CLAIMS

What is claimed is:

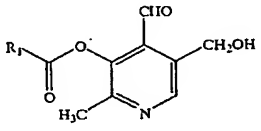
1. A pharmaceutical composition comprising: (a) a HMG CoA reductase inhibitor; (b) a vitamin B6 related compound; and (c) a pharmaceutically acceptable carrier.

2. The pharmaceutical composition according to claim 1 wherein the HMG CoA reductase inhibitor is selected from a group consisting: pravatstatin, lovastatin, fluvastatin, atorvastatin, simvastatin, rosuvastatin, velostatin, fluindostatin, and a mixture thereof.

3. The pharmaceutical composition according to claim 1 wherein the vitamin B6 related compound is selected from a group consisting: pyridoxal, pyridoxal-5'-phosphate, pyridoxamine, a 3-acylated analogue of pyridoxal, a 3-acylated analogue of pyridoxal-4,5-aminal, a pyridoxine phosphate analogue, and a mixture thereof.

4. The pharmaceutical composition according to claim 1 wherein the vitamin B6 related compound is pyridoxal-5-phosphate.

5. The pharmaceutical composition according to claim 3 wherein the 3-acylated analogue of pyridoxal is:



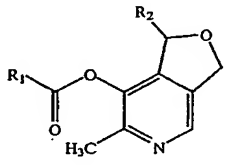
wherein,

R_1 is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

R_1 is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R_1 is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

6. The pharmaceutical composition according to claim 3 wherein the 3-acylated analogue of pyridoxal-4,5-aminal is



wherein,

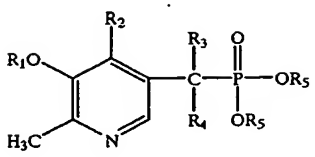
R_1 is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

R_1 is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R_1 is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

R_2 is a secondary amino group.

7. The pharmaceutical composition according to claim 3 wherein the pyridoxine phosphate analogue is selected from a group consisting:



(a)

wherein,

R_1 is hydrogen or alkyl;

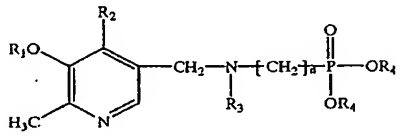
R_2 is –CHO-, -CH_2OH, -CH_3, -CO_2R6 in which R6 is hydrogen, alkyl, aryl; or

R_2 is –CH_2-O alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen and R_4 is hydroxy, halo, alkoxy, alkanoyloxy, alkylamino, or arylamino; or

R_3 and R_4 are halo; and

R_5 is hydrogen, alkyl, aryl, aralkyl, or –CO_2R_7 in which R_7 is hydrogen, alkyl, aryl, or aralkyl;



(b)

wherein,

R_1 is hydrogen or alkyl;

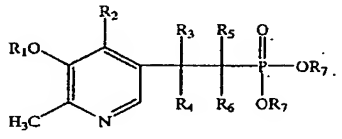
R_2 is –CHO, -CH_2OH, -CH_3, -CO_2R_5 in which R_5 is hydrogen, alkyl, aryl; or

R_2 is $-CH_2$-O alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen, alkyl, aryl, aralkyl,

R_4 is hydrogen, alkyl, aryl, aralkyl, or $-CO_2R6$ in which R6 is hydrogen, alkyl, aryl or aralkyl;

n is 1 to 6; and

(c) 

wherein,

R_1 is hydrogen or alkyl;

R_2 is –CHO-, CH_2OH-, $-CH_3$, $-CO_2R_8$ in which R_8 is hydrogen, alkyl, aryl; or

R_2 is $-CH_2$-O alkyl- in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen and R_4 is hydroxy, halo, alkoxy, or alkanoyloxy; or

R_3 and R_4 can be taken together to form =O;

R_5 and R6 are hydrogen; or

R_5 and R6 are halo;

R_7 is hydrogen, alkyl, aryl, aralkyl, or $-CO_2R_8$ in which R_8 is hydrogen, alkyl, aryl, or aralkyl.

8. A method for treating a patient at risk of cardiovascular disease comprising administering a therapeutically effective dose of the pharmaceutical composition according to any one of claims 1 to 7.

9. The method according to claim 8, wherein the patient is susceptible to hepatotoxicity.

10. The method according to claim 8 wherein the cardiovascular disease is selected from a group consisting: congestive heart failure, myocardial ischemia, arrhythmia, myocardial infarction, ischemic stroke, hemorrhagic stroke, coronary artery disease, hypertension (high blood pressure), atherosclerosis (clogging of the arteries), aneurysm, peripheral artery disease (PAD), thrombophlebitis (vein inflammation), diseases of the heart lining, diseases of the heart muscle, carditis, congestive heart failure, endocarditis, ischemic heart disease, valvular heart disease (malfunction of a valve or valves in the blood vessels of the heart), arteriosclerosis (hardening of the arteries), acute coronary syndrome (ACS), deep vein thrombosis (DVT), Kawazaki disease, high cholesterol, restinosis, late vein graft failure and heart transplant.

11. The method according to claim 8 wherein the dose of the HMG CoA reductase inhibitor is between 0.1 and 1000 mg per day.

12. The method according to claim 8 wherein the dose of the HMG CoA reductase inhibitor is 10 mg per day.

13. The method according to claim 8 wherein the dose of the HMG CoA reductase inhibitor is 20 mg per day.

14. The method according to claim 8 wherein the dose of the vitamin B6 related compound is between 0.1 to 50 mg/kg per day.

15. The method according to claim 8 wherein the dose of vitamin B6 related compound is between 1 to 15 mg/kg per day.

16. A method of a patient at risk for diabetes comprising administering a therapeutically effective dose of the pharmaceutical composition according to any one of claims 1 to 8.

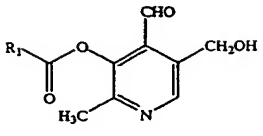
17. A method for treating a patient at risk of Alzheimer's disease comprising administering a therapeutically effective dose of the pharmaceutical composition according to any one of claims 1 to 7.

18. A method for treating a patient at risk of osteoporosis comprising administering a therapeutically effective dose of the pharmaceutical composition according to any one of claims 1 to 7.

19. A method of treating or preventing hypercholesterolemia in a patient, comprising administering a therapeutically effective dose of a vitamin B6 related compound wherein the vitamin B6 related compound is selected from a group consisting: pyridoxal-5'-phosphate, a 3-acylated analogue of pyridoxal, a 3-acylated analogue of pyridoxal-4,5-aminal, a pyridoxine phosphate analogue, and a mixture thereof.

20. The method according to claim 19 wherein the vitamin B6 related compound is pyridoxal-5-phosphate.

21. The method according to claim 19 wherein the 3-acylated analogue of pyridoxal is:



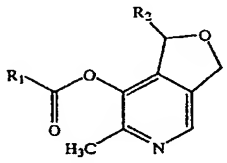
wherein,

R_1 is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

R_1 is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R_1 is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

22. The method according to claim 16 or 17 wherein the 3-acylated analogue of pyridoxal-4,5-aminal is



wherein,

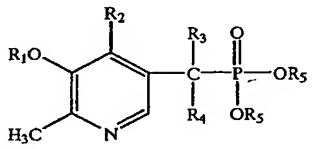
R_1 is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

R_1 is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R_1 is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

R_2 is a secondary amino group.

23. The pharmaceutical composition according to claim 16 wherein the pyridoxine phosphate analogue is selected from a group consisting:

(a) 

wherein,

R_1 is hydrogen or alkyl;

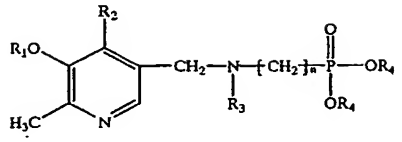
R_2 is –CHO-, -CH_2OH, -CH_3, -CO_2R6 in which R6 is hydrogen, alkyl, aryl; or

R_2 is –CH_2-O alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen and R_4 is hydroxy, halo, alkoxy, alkanoyloxy, alkylamino, or arylamino; or

R_3 and R_4 are halo; and

R_5 is hydrogen, alkyl, aryl, aralkyl, or –CO_2R_7 in which R_7 is hydrogen, alkyl, aryl, or aralkyl;



(b)

wherein,

R_1 is hydrogen or alkyl;

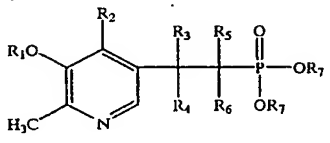
R_2 is –CHO, -CH_2OH, -CH_3, -CO_2R_5 in which R_5 is hydrogen, alkyl, aryl; or

R_2 is –CH_2-O alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen, alkyl, aryl, aralkyl,

R_4 is hydrogen, alkyl, aryl, aralkyl, or -CO_2R6 in which R6 is hydrogen, alkyl, aryl or aralkyl;

n is 1 to 6; and



(c)

wherein,

R_1 is hydrogen or alkyl;

R_2 is –CHO-, CH_2OH-, -CH_3, -CO_2R_8 in which R_8 is hydrogen, alkyl, aryl; or

R_2 is $-CH_2$-O alkyl- in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen and R_4 is hydroxy, halo, alkoxy, or alkanoyloxy; or

R_3 and R_4 can be taken together to form =O;

R_5 and R6 are hydrogen; or

R_5 and R6 are halo;

R_7 is hydrogen, alkyl, aryl, aralkyl, or $-CO_2R_8$ in which R_8 is hydrogen, alkyl, aryl, or aralkyl.

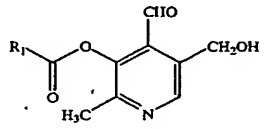
24. A method for treating a patient at risk of cardiovascular disease, said patient being administered a HMG CoA reductase inhibitor, comprising administering a therapeutically effective dose of a vitamin B6 related compound and a pharmaceutically acceptable carrier.

25. The method according to claim 24 wherein the HMG CoA reductase inhibitor is selected from a group consisting: pravastatin, lovastatin, fluvastatin, atorvastatin, simvastatin, rosuvastatin, velostatin, fluindostatin, and a mixture thereof.

26. The method according to claim 24 wherein the vitamin B6 related compound is selected from a group consisting: pyridoxal, pyridoxal-5'-phosphate, pyridoxamine, a 3-acylated analogue of pyridoxal, a 3-acylated analogue of pyridoxal-4,5-aminal, a pyridoxine phosphate analogue, and a mixture thereof.

27. The method according to claim 24 wherein the vitamin B6 related compound is pyridoxal-5-phosphate.

28. The method according to claim 27 wherein the 3-acylated analogue of pyridoxal is:



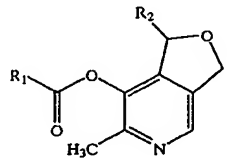
wherein,

R_1 is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

R_1 is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R_1 is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

29. The method according to claim 28 wherein the 3-acylated analogue of pyridoxal-4,5-aminal is



wherein,

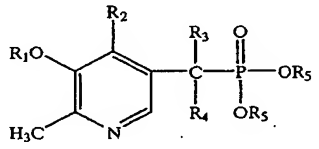
R_1 is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

R_1 is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R_1 is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

R_2 is a secondary amino group.

30. The method according to claim 28 wherein the pyridoxine phosphate analogue is selected from a group consisting:



(a)

wherein,

R_1 is hydrogen or alkyl;

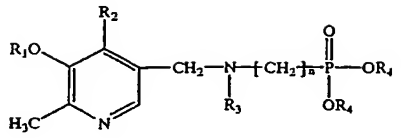
R_2 is –CHO-, -CH_2OH, -CH_3, -CO_2R6 in which R6 is hydrogen, alkyl, aryl; or

R_2 is –CH_2-O alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen and R_4 is hydroxy, halo, alkoxy, alkanoyloxy, alkylamino, or arylamino; or

R_3 and R_4 are halo; and

R_5 is hydrogen, alkyl, aryl, aralkyl, or –CO_2R_7 in which R_7 is hydrogen, alkyl, aryl, or aralkyl;



(b)

wherein,

R_1 is hydrogen or alkyl;

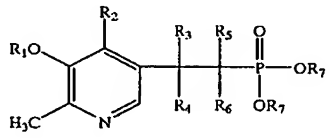
R_2 is –CHO, -CH_2OH, -CH_3, -CO_2R_5 in which R_5 is hydrogen, alkyl, aryl; or

R_2 is –CH_2-O alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen, alkyl, aryl, aralkyl,

R_4 is hydrogen, alkyl, aryl, aralkyl, or -CO_2R6 in which R6 is hydrogen, alkyl, aryl or aralkyl;

n is 1 to 6; and



(c)

wherein,

R_1 is hydrogen or alkyl;

R_2 is –CHO-, CH_2OH-, -CH_3, -CO_2R_8 in which R_8 is hydrogen, alkyl, aryl; or

R_2 is $-CH_2$-O alkyl- in which alkyl is covalently bonded to the oxygen at the 3-position instead of R_1;

R_3 is hydrogen and R_4 is hydroxy, halo, alkoxy, or alkanoyloxy; or

R_3 and R_4 can be taken together to form =O;

R_5 and R6 are hydrogen; or

R_5 and R6 are halo;

R_7 is hydrogen, alkyl, aryl, aralkyl, or $-CO_2R_8$ in which R_8 is hydrogen, alkyl, aryl, or aralkyl.

31. The method according to any one of claims 24 to 30, wherein the patient is susceptible to hepatotoxicity.

32. The method according to any one of claims 24 to 31 wherein the cardiovascular disease is selected from a group consisting: congestive heart failure, myocardial ischemia, arrhythmia, myocardial infarction, ischemic stroke, hemorrhagic stroke, coronary artery disease, hypertension (high blood pressure), atherosclerosis (clogging of the arteries), aneurysm, peripheral artery disease (PAD), thrombophlebitis (vein inflammation), diseases of the heart lining, diseases of the heart muscle, carditis, congestive heart failure, endocarditis, ischemic heart disease, valvular heart disease (malfunction of a valve or valves in the blood vessels of the heart), arteriosclerosis (hardening of the arteries), acute coronary syndrome (ACS), deep vein thrombosis (DVT), Kawazaki disease, high cholesterol, restinosis, late vein graft failure and heart transplant.

33. The method according to any one of claims 24 to 32 wherein the dose of the HMG CoA reductase inhibitor is between 0.1 and 1000 mg per day.

34. The method according to any one of claims 24 to 32 wherein the dose of the HMG CoA reductase inhibitor is 10 mg per day.

35. The method according to any one of claims 24 to 32 wherein the dose of the HMG CoA reductase inhibitor is 20 mg per day.

36. The method according to any one of claims 24 to 32 wherein the dose of the vitamin B6 related compound is between 0.1 to 50 mg/kg per day.

37. The method according to any one of claims 24 to 32 wherein the dose of vitamin B6 related compound is between 1 to 15 mg/kg per day.